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Health and Environmental Effects Profile for Allyl Alcohol

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR ALLYL ALCOHOL

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16. ABSTRACT

The Health and Environmental Effects Profile for allyl alcohol was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA) and to provide health-related limits for emergency actions under Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Allyl alcohol has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for allyl alcohol is 0.34 mg/day for oral exposure.

The Reportable Quantity (RQ) value of 1, 10, 100, 1000 or 5000 pounds is used to determine the quantity of a hazardous substance for which notification is required in the event of a release as specified by CERCLA based on chronic toxicity. The RQ value for allyl alcohol is 100.

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PREFACE

The first draft of this document was prepared by Syracuse Research Corporation under Contract No. 68-03-3228. This document was subsequently reviewed and revised by ECAO-Cincinnati and the OHEA offices of CAG, EAG and REAG.

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LIST OF ABBREVIATIONS

ADH	Alcohol dehydrogenase
ADI	Acceptable daily intake
BCF	Bioconcentration factor
BOD	Biological oxygen demand
BODT	Biological oxygen demand theoretical
cAMP	Cyclic 3,5-adenosine monophosphate
CAS	Chemical Abstracts Service
CNS	Central nervous system
CS	Composite score
DMSO	Dimethyl sulfoxide
EC_{50}	Effective concentration to 50% of recipients
ED_{10}	Effective dose to 10% of recipients
GDH	Glutamate dehydrogenase
GI	Gastrointestinal
GOT	Glutamic oxaloacetic transaminase
GPT	Glutamic pyruvic transaminase
GSH	Reduced glutathione
K_{ow}	Octanol/water partition coefficient
Koc	Soil sorption coefficient
LC_{50}	Concentration lethal to 50% of recipients
LD_{50}	Dose lethal to 50% of recipients
LDH	Lactate dehydrogenase
LOAEL	Lowest-observed-adverse-effect level
MDH	Malate dehydragenase
MED	Minimum effective dose

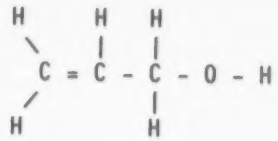
LIST OF ABBREVIATIONS (cont.)

NAD^+	Nicotine-adenine-dinucleotide
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
PAT	Promoting Activity Test
ppm	Parts per million
RD_{50}	Concentration necessary to depress the respiratory rate by 50%
RQ	Reportable quantity
RV_d	Dose-rating value
RV_e	Effect-rating value
SDH	Succinic dehydrogenase
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamic pyruvic transaminase
STEL	Short-term exposure level
THOD	Theoretical oxygen demand
TLV	Threshold Limit Value
TSS	Thymidine Incorporation Inhibiting Screening Test
TWA	Time-weighted average
UDP	Uridine diphosphate
UDPGA	Uridine diphosphate-glucuronic acid
UV	Ultraviolet
v/v	Volume per volume
WS	Water solubility

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

The chemical commonly known as allyl alcohol is also known by the synonyms 2-propen-1-ol, vinyl carbinol, propenyl alcohol and 1-propen-3-ol. The structure, molecular weight, and empirical formula of this compound are as follows:



Molecular weight: 58.08

Empirical formula: C_3H_6O

The CAS Registry number for allyl alcohol is 107-18-6.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Allyl alcohol is a colorless, mobile liquid with a pungent odor that can be irritating to eyes and mucous membranes (Beacham, 1978). Selected physical properties are as follows:

Melting point:	-129°C (Beacham, 1978)
Boiling point:	96.9°C (Beacham, 1978)
Specific gravity, 20/4°C:	0.8520 (Beacham, 1978)
Refractive Index, 20°C:	1.4127 (Beacham, 1978)
Vapor pressure, mm Hg:	
at 30°C	32 (Verschueren, 1983)
at 25°C	23.8 (TSCA-ITC, 1984)
at 21.7°C	20 (Perry and Chilton, 1973)
at 20°C	19 (Beacham, 1978)
at 10.5°C	10 (Perry and Chilton, 1973)
at 0.2°C	5 (Perry and Chilton, 1973)
at -20.0°C	1 (Perry and Chilton, 1973)
Water solubility:	miscible (Hawley, 1977)

Nonaqueous solubility:	miscible with all common organic solvents (Martin and Worthing, 1977)
Log octanol/water partition coefficient:	0.17 (Hansch and Leo, 1979)
Flashpoint (open cup):	32.2°C (Martin and Worthing, 1977)
Conversion factors (air) at 20°C:	1 mg/m³ = 0.414 ppm 1 ppm = 2.414 mg/m³ (Verschueren, 1983)

Chemically, allyl alcohol has a tendency to polymerize on storage (Martin and Worthing, 1977) and, therefore, may require the addition of a stabilizer (Hartley and Kidd, 1983). It is stable in UV light (Hartley and Kidd, 1983). Allyl alcohol forms a wide variety of compounds by addition to the olefinic bond as well as other characteristic derivatives of alcohols. The reactivity of allyl alcohol as an alcohol in replacement reactions is considerably greater than that of the saturated primary alcohols; in many instances, its reactivity as an olefin is also greater than that of simple olefins, although the reverse is sometimes the case (Vesper, 1947).

1.3. PRODUCTION DATA

Currently, the sole industrial manufacturer of allyl alcohol in the United States is the FMC Corporation in Bayport, TX (SRI, 1984; USITC, 1984). Until about 1980, Shell Chemical manufactured allyl alcohol, which was primarily used captively to make synthetic glycerine. Available production data for 1977 (U.S. EPA, 1977) are listed in Table 1-1. Import and export figures are not available.

Allyl alcohol has been produced commercially in the United States by three different processes (Beacham, 1978). In the first commercial process, which was introduced in 1947, allyl chloride is hydrolyzed to allyl alcohol under alkaline conditions using steam injection. The second process, used by Shell to make glycerin, involves the oxidation of propylene to acrolein,

TABLE 1-1

Allyl Alcohol Production Data*

Producer	Type	1977 Production
FMC Corp. Pasadena, TX	manufacturer	10-50 million lbs
Shell Chemical Norco, LA Deer Park, TX	manufacturer manufacturer	10-50 million lbs 1-10 million lbs
Haven Chemical Philadelphia, PA	manufacturer	1-10 thousand lbs

*Source: U.S. EPA, 1977

which is reacted with a secondary alcohol to yield allyl alcohol and a ketone; the allyl alcohol formed is not isolated, but is converted directly to glycerin by hydrogen peroxide reaction. In the third process, allyl alcohol is made by isomerization of propylene oxide over a lithium phosphate catalyst.

1.4. USE DATA

The production of glycerin was the major use of allyl alcohol until Shell Chemical closed their production facilities. About 22 million pounds of allyl alcohol is annually consumed for other uses (Beacham, 1978). The major current use of allyl alcohol is probably the production of allyl esters, such as diallyl phthalate. Also, allyl alcohol is used commercially in the production of resins and polymers (Beacham, 1978). Allyl alcohol has been sold as a pesticide for seed bed sterilization (Beacham, 1978) and as a herbicide for the control of weed and grass seeds (Hartley and Kidd, 1983). The significance of the current use of allyl alcohol as a pesticide is not certain. Use as a military poison gas and as an intermediate for pharmaceutical and organic syntheses has also been cited (Hawley, 1977).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Like other chemicals, the fate of allyl alcohol in the environment will depend on its ability to undergo chemical, photochemical and biological reactions and to transport or partition from one environmental matrix into another. The individual fate processes are discussed below.

2.1. WATER

2.1.1. Hydrolysis. Alcohols are generally resistant to hydrolysis (Lyman et. al., 1982); in addition, the allyl group of allyl alcohol does not appear likely to be hydrolyzed in the aquatic environment. Therefore, the environmental hydrolysis of allyl alcohol is probably insignificant.

2.1.2. Oxidation. Chemical oxidation of organic chemicals in aquatic environments may be due to oxidants, such as singlet oxygen, alkyl peroxyl radical ($RO_2\cdot$), alkoxy radical ($RO\cdot$) or hydroxyl radical ($\cdot OH$), which are generated primarily by sunlight photooxidation (Mabey et al., 1981). The rate constant for the aqueous reaction (pH 7) of allyl alcohol with hydroxyl radicals at room temperature has been reported to be 1.2×10^9 M^{-1} sec^{-1} (Anbar and Neta, 1967) and 1.97×10^9 M^{-1} sec^{-1} (Dorfman and Adams, 1973). Assuming an environmental OH radical concentration of 10^{-17} M, the half-life for allyl alcohol reaction with OH radicals can be calculated to be ~500-600 days, which is not very rapid. Reaction of the alkyl peroxyl radical or singlet oxygen with olefinic moieties may have some environmental importance (Mabey et al., 1981); however, the importance of these oxidations with allyl alcohol has not been examined experimentally.

2.1.3. Photooxidation. Knoevenagel and Himmelreich (1976) studied the photooxidation of various organic compounds in water in a specially designed laboratory apparatus that was irradiated with UV light from a high pressure

Hg-vapor lamp; air was pumped continually into the water solution. Allyl alcohol was degraded to 86% of its initial concentration in a 24-hour test period; however, the wavelength range of the UV light was not reported. While the photooxidation of allyl alcohol in the aquatic environment may occur, no currently available evidence suggests that this mechanism will occur at a relatively rapid rate in the environment.

2.1.4. Microbial Degradation. Bridie et al. (1979a) used the effluent from a waste treatment plant to determine a 5-day BOD of allyl alcohol to be 81% of the THOD. Mills and Stack (1954) determined a 10-day BOD of allyl alcohol to be 73% of the THOD, while Stafford and Northrup (1955) reported a 5-day BODT of 20%. Using a settled sewage seed, Ettinger (1956) determined 5-, 10-, 15- and 20-day BODTs of allyl alcohol to 9.1, 55.0, 78.2 and 81.8%, respectively. Wagner (1976) used a respirometric dilution method, with domestic sewage as microbial inoculum, to determine a 5-day BODT of 69%. Sasaki (1978) reported that the Japanese MITI test confirms that allyl alcohol is "well-biodegradable" because oxygen consumption exceeds 30% after 2 weeks of biodegradation. Thom and Agg (1975) reported that allyl alcohol should be degradable by biological sewage treatment with appropriate acclimatization.

Fridman et al. (1984) developed active strains of bacteria, primarily Pseudomonas and Micrococcus, which are effective in degrading 4000 ppm concentrations of allyl alcohol in wastewaters. Crude, cell-free preparations of the fungus, Botrytis cinerea, have been found to rapidly oxidize allyl alcohol (Fukuda and Brannon, 1971).

By using a BOD determination, allyl alcohol degradation in river water at 20°C was found to be 50-80% in 5 days after 1-5 days of acclimatization (Sago, 1965).

2.1.5. Transport. The transport of allyl alcohol in the aquatic environment will depend on the ability of the compound to volatilize, to adsorb onto particulate organic matter and sediment, and to bioaccumulate in aquatic organisms.

2.1.5.1. VOLATILIZATION -- Allyl alcohol and water are completely miscible (Hawley, 1977) and the vapor pressures of both at 25°C are nearly the same (23.8 mm Hg) (Perry and Chilton, 1973). Hine and Mookerjee (1975) reported that a dilute aqueous solution of allyl alcohol at equilibrium at 25°C has a concentration in the water-phase to concentration in the gas-phase ratio of 7762:1. The inverse of this ratio, 1.3×10^{-4}, is the unitless Henry's Law constant. Conversion to units, using an RT value of 2.40×10^{-2} m^3-atm/mol (where R is the gas constant and T is temperature in °K), yields a Henry's Law constant of 3.1×10^{-6} m^3-atm/mol. This value suggests that allyl alcohol will volatilize slowly from the aquatic environment. The evaporation may be more significant in shallow water bodies (Lyman et al., 1982).

2.1.5.2. AQUATIC ADSORPTION -- Experimental data regarding the adsorption of allyl alcohol to particulate matter and sediment in water were not located in the available literature; however, the complete water solubility of allyl alcohol and its easy leaching in soils (Section 2.3.) suggest that partitioning of allyl alcohol from the water column to sediments or particulates is not likely to be significant.

2.1.5.3. BIOACCUMULATION -- Experimental bioconcentration data with respect to aquatic organisms were not located in the available literature. The complete water solubility and low log K_{ow} (0.17) (Hansch and Leo, 1979) of allyl alcohol predict that bioaccumulation in aquatic organisms

will not have environmental importance. The BCF of an organic compound may be estimated from the WS or from the K_{ow} by the following equations:

$$\log BCF = 2.791-0.564 \log WS \text{ (in ppm)} \text{ (Kenaga and Goring, 1978)} \quad (2\text{-}1)$$

$$\log BCF = 0.76 \log K_{ow}-0.23 \text{ (Veith et al., 1980)} \quad (2\text{-}2)$$

Assuming WS is 10^6 ppm, the BCF values calculated from Equations 2-1 and 2-2 are 0.3 and 0.8, respectively.

Scheunert et al. (1981) observed no significant uptake of allyl alcohol in lettuce and carrots planted in greenhouse soils treated with the compound.

2.2. AIR

The atmospheric chemical removal processes include reaction with hydroxyl radicals, reaction with other radicals, reaction with ozone, and photolytic transformations (Cupitt, 1980). Lloyd (1978) reported the rate of reaction of hydroxyl radicals (assuming an atmospheric concentration of 10^6 molecules/cm^3) with allyl alcohol at 27°C to be 9.3% per hour. Therefore, the removal of allyl alcohol from the atmosphere by OH radicals can be expected to be significant and rapid. Pertinent data regarding the reaction of allyl alcohol with other radicals or with ozone under environmental conditions were not located in the available literature as cited in the Appendix.

Hustert and Parlar (1981) examined the gas-phase photochemical degradation of volatile alkanes, alkenes, aromatics, alcohols, ketones and other compounds in the laboratory using initial concentrations of $4.1x10^{-6}$ M.

Significant photolysis of allyl alcohol did not occur at wavelengths >300 nm during 2 hours of irradiation. At 230-300 nm, 39.7% of the allyl alcohol was degraded to CO and CO_2 during the 2-hour irradiation period. This may suggest that the direct photolysis of allyl alcohol in the ambient atmosphere is not significant in comparison with its reaction with OH radical.

The atmospheric physical removal processes include dissolution (wet deposition), adsorption on aerosol particles and dry deposition (Cupitt, 1980). The complete miscibility of allyl alcohol and water suggest that removal by rainfall may have some importance on a localized level; however, this process cannot be expected to be as important as chemical removal by OH radicals. The vapor pressure of allyl alcohol is too high for adsorption on aerosol particles to have any significance. This conclusion is based on suggestions by Cupitt (1980) that vapor-phase adsorption is important only for compounds having saturation vapor pressures of $\leq 10^{-7}$ mm Hg. Removal of allyl alcohol from the atmosphere by dry deposition is unlikely to be significant.

2.3. SOIL

2.3.1. Microbial Degradation. Jensen (1959, 1961) determined in laboratory experiments that the following soil microorganisms are capable of metabolizing allyl alcohol: Pseudomonas fluorescens, Nocardia corallina, Trichoderma viride and some species of Azotobacter. In addition, it was determined in soil studies that the herbicidal action of allyl alcohol disappears from the soil in 4-8 days; however, when the soil was sterilized before allyl alcohol application, the herbicidal activity persisted for 3-4 weeks or longer. Jackson (1971, 1973) also found that the soil microbe, Trichoderma viride, is capable of rapidly metabolizing allyl alcohol; acrylate and acetate were found to be metabolites.

2.3.2. Chemical Degradation. Pertinent data regarding the chemical degradation of allyl alcohol in the soil were not located in the available literature as cited in the Appendix.

2.3.3. Transport. The leaching of allyl alcohol was examined in soil column tests by Scheunert et al. (1981). As indicated in Table 2-1, the allyl alcohol was leached readily, but leaching was retarded with an increased organic matter content of the soil.

The complete WS and low K_{ow} value of allyl alcohol suggest that it will be highly mobile and, therefore, easily leached in soil. A K_{oc} for allyl alcohol can be estimated from the following equations using the WS and the K_{ow}:

$$\log K_{oc} = 3.64-0.55 \log WS \text{ (in ppm) (Kenaga and Goring, 1978)} \quad (2-3)$$

$$\log K_{oc} = 0.544 \log K_{ow}+1.377 \text{ (Kenaga and Goring, 1978)} \quad (2-4)$$

Assuming WS is 10^6 ppm, the K_{oc} values calculated from Equations 2-3 and 2-4 are 2 and 29, respectively. The soil sorption can also be predicted from molecular topology and quantitative structure-activity relationships in a method presented by Sabljic (1984). Using the formula for the molecular connectivity index and the log K_{oc} equation given by Sabljic (1984), a K_{oc} value of 32 is predicted for allyl alcohol. K_{oc} values of <50 indicate high soil mobility.

The relatively high vapor pressure and low soil sorption of allyl alcohol suggest that volatilization from soil may be significant. In greenhouse studies with unirrigated soil, Scheunert et al.(1981) observed that

TABLE 2-1

Results of ^{14}C-Labeled Allyl Alcohol Tests*

Soil Type	Organic Content (%)	Percent of Applied Leached After 2 Days
Sand soil #1	0.51	100
Sand soil #2	2.89	83.3
Sandy loam	1.00	98.6

*Source: Scheunert et al., 1981

disappearance of allyl alcohol from the soil was due predominantly to volatilization. Hartley and Kidd (1983) reported that disappearance of allyl alcohol from soil was due primarily to evaporation; however, evaporation from moist soils is more complex, and may be inhibited due to the complete WS and subsequent leaching.

2.3.4. Persistence. In greenhouse studies with unirrigated soil (sandy loam), Scheunert et al. (1981) determined that only an average of 12.5% of the applied ^{14}C-allyl alcohol radioactivity remained in the soil after an 8-day interval between application and sowing. The amount of unchanged allyl alcohol was not quantified due to the analytical methods used; therefore, part of the remaining radioactivity may have been degradation products. The greenhouse soil was then planted with lettuce and carrots and irrigated; the radioactive residues showed little leaching and, to a high percentage, were unextractable.

Jensen (1961) found that the herbicidal activity of allyl alcohol disappeared from soil in 4-8 days, but the activity persisted for $\geq$3-4 weeks or longer in soil sterilized before application.

It has also been reported that allyl alcohol disappears from soil within 3-10 days (Hartley and Kidd, 1983) or within 7-9 days (Shell, n.d.).

2.4. SUMMARY

The available data suggest that microbial degradation may be a primary pathway by which allyl alcohol is removed from the aquatic environment. Loss by volatilization may have some significance, with photochemical oxidation contributing to aqueous disappearance to a limited degree. Hydrolysis, bioaccumulation and adsorption are not likely to be important in the aquatic environment.

Allyl alcohol exposed to the ambient atmosphere will react rapidly with hydroxyl radicals in the air, with a projected half-life of <1 day to several days, depending on temperature and hydroxyl radical concentration. Atmospheric removal by rainfall (dissolution) may have limited importance.

In the soil environment, allyl alcohol does not appear to be a persistent chemical, as complete disappearance in <2 weeks has been reported. Removal by volatilization and microbial degradation appear to be the significant processes. Allyl alcohol may be leached easily in most types of soil, particularly those with low organic content.

In summary, allyl alcohol is not expected to persist in the environment; the lack of ambient monitoring data in Chapter 3 support this conclusion.

3. EXPOSURE

3.1. WATER

The U.S. EPA STORET Data Base contains no observations for allyl alcohol. Other environmental monitoring data were not located in the available literature as cited in the Appendix.

Environmental contamination of water by allyl alcohol may occur from aqueous waste stream releases from production facilities (TSCA-ITC, 1984), from use facilities, and from agricultural runoff from soils treated with allyl alcohol.

3.2. FOOD

Pertinent data regarding monitoring of allyl alcohol in ready-to-eat foods were not located in the available literature as cited in the Appendix. Scheunert et al. (1981) observed no uptake of allyl alcohol in lettuce and carrots planted in greenhouse soils treated with the compound.

3.3. INHALATION

Pertinent data regarding the monitoring of allyl alcohol in the ambient atmosphere were not located in the available literature as cited in the Appendix. Rigby (1981) detected allyl alcohol in the organic volatiles emitted from heated plastics; allyl alcohol is used as an intermediate in the production of various polymers and resins (see Section 1.4.).

Fugitive gaseous emissions from production facilities may release allyl alcohol to the atmosphere (TSCA-ITC, 1984). Volatilization from soils treated with allyl alcohol may also be a source of exposure.

3.4. DERMAL

Pertinent data regarding dermal exposure to allyl alcohol under ambient conditions were not located in the available literature as cited in the Appendix.

4. PHARMACOKINETICS

4.1. ABSORPTION

Gastrointestinal and respiratory tract absorption of allyl alcohol can be inferred from systemic toxicity observed in laboratory animals following oral and inhalation exposure to the chemical (Sections 5.5. and 5.6.). Based on the rapid onset of toxic effects following acute oral and inhalation exposures, von Oettinger (1943) concluded that absorption was rapid. Kodama and Hine (1958) reported peak hepatic portal vein levels of allyl alcohol at 30-60 minutes after a single gavage dose (120 mg/kg in distilled water) in rats, indicating that rapid GI absorption occurred. Based on the acute lethality levels of allyl alcohol (see Table 5-5) following oral and dermal exposure compared with intravenous and intraperitoneal injection, both natural routes of absorption appear to be quite efficient (for further discussion see Section 5.6.). Absorption also occurs by the dermal route at levels sufficient to cause toxicity (Dehn, 1981; Dunlap et al., 1958; Kaye and Young, 1972; Shell Chemical Corp., n.d.).

4.2. DISTRIBUTION

Following absorption or injection into the blood, allyl alcohol is expected to be distributed throughout the body while its metabolism (Section 4.3.) appears to occur primarily in the liver. Kodama and Hine (1958) measured blood levels of allyl alcohol in the hepatic portal vein of rats following oral and intravenous treatment. Mean blood levels of allyl alcohol were elevated between 9 and 15 µg/mℓ during the interval of 15-120 minutes after a single oral dose (120 mg/kg in distilled water). Maximum blood levels occurred at 30-60 minutes after dosing. Blood levels of allyl alcohol following intravenous infusion (30 mg/kg) were initially high (average ~24 µg/mℓ blood) but decreased rapidly (to ~4 µg/mℓ)

within 15 minutes and were almost cleared completely within 1 hour. These data indicate that there is no apparent accumulation of the parent compound following brief exposures (Browning 1965).

4.3. METABOLISM

Metabolism of allyl alcohol proceeds primarily by oxidation, mediated by ADH, to acrolein (Serafini-Cessi, 1972; Patel et al., 1980a,b, 1983). Serafini-Cessi (1972) demonstrated the conversion of allyl alcohol, *in vitro*, to acrolein using ADHs from postmitochondrial fractions or whole liver homogenates. The co-factor NAD^+ was required. Patel et al. (1980a,b, 1983) demonstrated the metabolism of allyl alcohol to acrolein and further to acrylic acid, *in vitro*, by rat liver microsomal or cytosol preparations in the presence of NAD^+. Other routes of metabolism of allyl alcohol include its epoxidation to glycidol or the epoxidation of acrolein to glycidaldehyde (Patel et al., 1980a,b). Both epoxide compounds can be further oxidized by rat liver microsomes to glycerol and glyceraldehyde, respectively. A summary of the proposed pathways of hepatic metabolism of allyl alcohol, determined *in vitro*, is presented in Figure 4-1 (Patel et al. 1980a).

Oxidation of allyl alcohol apparently proceeds rapidly. Winer (1958) reported that allyl alcohol is an excellent substrate for ADH. Kodama and Hine (1958) administered 30 mg allyl alcohol/kg to rats by intravenous injection and monitored its disappearance from the blood. Immediately after injection, blood levels reached 24 µg allyl alcohol/mℓ blood but were decreased to 4 µg/mℓ within 15 minutes. Within 1 hour, allyl alcohol had been completely metabolized. Using constant intravenous infusion and monitoring blood allyl alcohol levels, Kodama and Hine (1958) calculated the rate of metabolism to be 23-24 mg/kg/hour in rats.

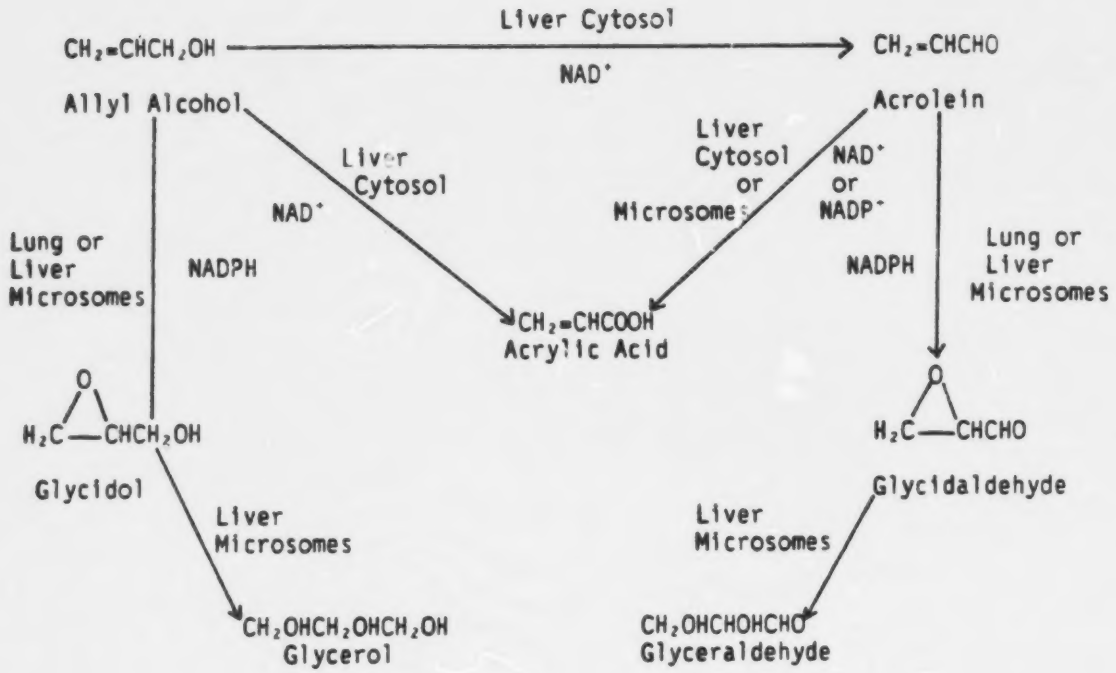


FIGURE 4-1

In Vitro Pathways of Biotransformation of Allyl Alcohol and Acrolein in Lung and Liver Preparations

Source: Patel et al., 1980a

The major site of allyl alcohol oxidation is the liver. Reid (1972) demonstrated the very limited metabolism of allyl alcohol in the lungs and kidney compared with the liver. Reid (1972) administered ^{14}C-labeled allyl alcohol (sp. act. 2.46 mCi/mmol; position of label not specified) to male Sprague-Dawley rats (200 g) by intraperitoneal injections at 0.05 mℓ/kg. Twenty-four hours after the administration of ^{14}C-allyl alcohol, livers of test animals showed extensive periportal necrosis on histological examination. No necrosis was observed in lungs and kidneys. Binding studies showed that radioactivity equivalent to ~120 pmol of allyl alcohol/g of protein was bound in the liver after 8 hours, and one-half that amount after 24 hours (Table 4-1, control data). As demonstrated by autoradiography, most of the binding in the liver occurred in the periportal area, with little binding in the antrilobular area. Little binding was observed in the lungs (10.5-16.1 pmoles/mg protein) and kidneys (3.6-13.6 pmoles/mg protein) (see Table 4-1). When the rats were pretreated with pyrazole, an inhibitor of ADH, binding in the liver and lungs was significantly reduced, indicating that binding and necrosis were mediated by a metabolite, presumably acrolein. Pretreatment of the rats with phenobarbital, an inducer of microsomal enzymes, had little effect. Ferguson et al. (1966) reported that allyl alcohol was "fairly well utilized" in the ovary, testis and adrenal gland, but relative rates of metabolism were not reported.

The conjugation of allyl alcohol or its metabolites with glutathione has been demonstrated in vivo in rats (Siegers, 1981). Kaye and Young (1972) and Kaye (1973) detected 3-hydroxypropylmercapturic acid in the urine of rats given allyl alcohol (in arachis oil) by subcutaneous injection. A group of 72 male CFE rats received a total dose of 0.613 g of allyl alcohol

TABLE 4-1

Binding of ^{14}C-Allyl Alcohol:
Effect of Pyrazole or Phenobarbital Treatment[a]

Treatment (number)	Time of Killing (hours)	Concentration of Bound Radioactivity (pmol/mg protein)		
		Liver	Lung	Kidney
Control (5)	08.00	119.5±36.7	16.1±3.6	10.7±2.3
Pyrazole (2)	08.00	21.6± 0.6[b]	11.2±1.7	4.2±0.8
Control (2)	24.00	80.2±10.2	10.5±0.9	3.6±0.9
Pyrazole (2)	24.00	12.9± 0.4[b]	4.9±0.5[b]	2.4±0.3
Control (3)	06.00	80.2± 7.9	12.3±0.8	13.6±1.5
Phenobarbital(3)	06.00	57.2± 2.8	9.7±0.6	12.4±1.0

[a]Source: Reid, 1972

[b]Significantly different from controls at 5% level. Number of rats per group (N) given in parentheses.

(1 mℓ of 1% solution per rat), and within 24 hours 0.255 g of the dicyclohexyl ammonium salt of 3-hydroxypropylmercapturic acid was recovered. This represented a 6.3% conversion of the allyl alcohol dose to the mercapturic acid conjugate. No other conjugate metabolites were identified. The authors (Kaye and Young 1972; Kaye, 1973) suggested that allyl alcohol was oxidized to a carbonyl-containing metabolite (such as acrolein), which conjugated with glutathione. Watkins and Klaassen (1983) reported a slight decrease in the level of hepatic UDPGA in rats pretreated with allyl alcohol (0.05 mg/kg intraperitoneally), which may reflect its use in a conjugation process.

Several studies have been conducted that attribute the localized periportal hepatic necrosis caused by allyl alcohol (Sections 5.5. and 5.6.) to its primary metabolite, acrolein. ADH appears to be localized primarily in the periportal hepatocytes where allyl alcohol is presumed to be oxidized to acrolein (Reid, 1972). Acrolein has been shown to bind to macromolecules (Schon and Steidl, 1957; Rees and Tarlow, 1967) and is thought to be primarily responsible for the hepatotoxic effects of allyl alcohol. As discussed previously, inhibitors of ADH (pyrazole) reduce the amount of reactive metabolite binding to proteins while phenobarbital pretreatment had little effect on allyl alcohol metabolism (see Table 4-1) (Reid, 1972). Hansen and Anders (1978) and Siegers et al. (1977) reported that detoxification of acrolein by glutathione conjugation is important in abating allyl alcohol hepatotoxicity since rats pretreated with diethyl maleate (reduced glutathione levels) were severely susceptible to allyl alcohol hepatotoxicity. Studying the oxidation of allyl alcohol in the periportal and centrilobular regions of the liver, Belinsky et al. (1984) reported metabolism rates of 31 and 23 μmol/g/hour, respectively; these values do not support the absolute

localization of the hepatic metabolism of allyl alcohol in the periportal region. Belinsky et al. (1984) concluded that periportal hepatocytes were more sensitive to acrolein, possibly through inhibition of mitochondrial respiration enzymes.

4.4. EXCRETION

Data regarding the excretion of allyl alcohol and its metabolites are limited. Browning (1965) reported that no parent compound was excreted in the urine of animals treated by subcutaneous or intravenous injection. Kaye (1973) studied the excretion of mercapturic acid metabolites in urine of rats that were given allyl alcohol by subcutaneous injection. A total dose of 0.613 g allyl alcohol was given to a group of 72 rats, and 3-hydroxypropyl mercapturic acid was recovered in the urine. After 24 hours, the conjugate accounted for 6.3% of the administered dose.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of allyl alcohol were not located in the available literature as cited in the Appendix.

Allyl alcohol epoxidation (see Section 4.3.) produces glycidaldehyde, which has been found to be a weak skin carcinogen in mice (Van Duuren et al., 1965). The extent of allyl alcohol epoxidation to glycidaldehyde has not been determined, hence, this finding may be irrelevant to the carcinogenicity of the parent compound.

5.2. MUTAGENICITY

The mutagenicity of allyl alcohol has been tested in several microbial species, with and without metabolic activation (Table 5-1). As seen in the table, Carere and Morpurgo (1981) found allyl alcohol negative in Salmonella, Streptomyces and Aspergillus under a variety of test conditions. Negative results were also obtained in Salmonella TA100 place incorporation assay (Yamaguchi, 1980). Lijinsky and Andrews (1980) tested allyl alcohol in the five standard Salmonella strains using a variety of treatment conditions (i.e., plate and pre-incubation, water and DMSO as solvents) and reported marginal positive results only in TA1535 in the pre-incubation assay with distilled water as the solvent and with hamster S-9. Lutz et al. (1982), using only TA100, reported positive results in a pre-incubation assay, however, the positive response was observed only without rat S-9. The discussion of this paper notes that allyl alcohol was negative in the plate test and the authors speculate that allyl alcohol may be oxidized to acrolein under the pre-incubation conditions.

TABLE 5-1

Mutagenicity Testing of Allyl Alcohol

Assay	Indicator/ Organism	Application	Concentration or Dose	Activating System	Response	Comment	Reference
Reverse mutation	Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100	plate incorporation and liquid incubation	NR	±S9	+/-	Marginally positive effect observed only when allyl alcohol dissolved in water, not Me_2SO, in liquid incubation assay. Maximum nontoxic dose 500 µg/plate. The response was positive only in the presence of S-9.	Lijinsky and Andrews, 1980
Reverse mutation	S. typhimurium TA1535, TA1537, TA1538, TA98, TA100	spot test	0.05 µg/plate	±S9	-	NC	Carere and Morpurgo, 1981
Reverse mutation	S.typhimurium TA1535, TA100	plate incorporation	0.025-0.1 µg/plate	±S9	-	NC	Carere and Morpurgo, 1981
Reverse mutation	S. typhimurium TA100	plate incorporation	200 µg/plate	none	-	Sample dissolved in DMSO	Yamaguchi, 1980
Reverse mutation	S. typhimurium TA100	liquid incubation	0-0.3 µmol/mL	±S9	+/-	Potent mutagen in absence of S-9. In presence of S-9, negative. Also negative in plate test without S-9.	Lutz et al., 1982
Forward mutation	Streptomyces coelicolor A3	plate incorporation	2-100 µL/plate	none	-	NC	Carere and Morpurgo, 1981; Principe et al., 1981
Forward mutation	Aspergillus nidulans haploid strain 35	plate incorporation	10-40 µL/plate	none	-	NC	Carere and Morpurgo, 1981

NR = Not reported; NC = no comment

5.3. TERATOGENICITY

In a German study (Roschlau and Rodenkirchen, 1969) available as an English abstract, the effect of allyl alcohol on fetal development was examined in mice. Pregnant mice were given allyl alcohol (dose not reported) by three routes (subcutaneously, intraperitoneally or orally) on day 16 or 18 of gestation. All animals were killed on day 19 of gestation so that either 24 or 72 hours had elapsed since treatment. Intraperitoneal dosing caused severe toxicity and produced high rates of fetal mortality. Hepatic necrosis with dilatations of the sinusoids was reported in fetuses treated on day 18 of gestation. These toxic effects were not seen in fetuses exposed on day 16 of gestation, which suggest a reversible effect or a sensitive developmental stage at 18 days.

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other reproductive effects of allyl alcohol were not located in the available literature as cited in the Appendix.

5.5. CHRONIC TOXICITY

A number of subchronic toxicity tests using oral and inhalation exposure have been conducted. No chronic tests conducted for the majority of an animals lifespan were located in the available literature as cited in the Appendix.

Dunlap et al. (1958) administered allyl alcohol at 1, 5, 50, 100, 250, 500 or 1000 ppm (mg/ℓ) to Long-Evans rats (10 animals of each sex/dose level) in the drinking water for 90 days. Similar groups served as controls. Based on water consumption data, these concentrations were equivalent to doses of 0.13, 0.62, 5.9, 11.6, 25.5, 41.0 and 72.0 mg/kg/day, respectively, for males and 0.17, 0.94, 7.34, 13.2, 34.0, 43.7 and 67.4 mg/kg/day, respectively, for females. At the two higher concentrations,

body weight gain was decreased in males and females. Fluid intake decreased with increasing concentration of allyl alcohol. After 13 weeks, the rats were killed and autopsied. Significantly ($p<0.05$) increased relative liver weights were seen at 250 and 1000 mg/ℓ in males. Significantly ($p<0.05$) increased relative kidney weights were observed in both sexes at $\geq$250 mg/ℓ. No effects were seen in rats at concentrations $\leq$100 mg/ℓ. Peritoneal fat was decreased in the 500 mg/ℓ group and was absent in the 1000 mg/ℓ group (sex not specified). Additional evidence of hepatic toxicity included pale-yellowish discoloration and spongy liver texture in 2/10 females at 1000 mg/ℓ. Livers of these rats showed well-localized areas of necrosis with evidence of regeneration. Other effects that may or may not have been treatment-related included respiratory disease, "crustiness of the eyelids," and emaciation in two male rats at 250 mg/ℓ (one had pulmonary edema, one had necrosis of intestinal mucosa at necropsy).

Carpanini et al. (1978) exposed groups of 15 male and 15 female Wistar rats to drinking water containing 0, 50, 100, 200 or 800 ppm (mg/ℓ) allyl alcohol for 15 weeks. Based on water consumption data, these concentrations were equivalent to dosages of 0, 4.8, 8.3, 14.0 and 48.2 mg/kg/day for males, respectively, and 0, 6.2, 6.9, 17.1 and 58.4 mg/kg/day, respectively, for females. Food intake and growth were depressed in males treated at 200 and 800 mg/ℓ and in females at 800 mg/ℓ. A dose-related decrease in water consumption was seen at all concentrations. Results of hematologic and clinical chemistry tests were unremarkable. Several tests of renal function were performed. In a concentration test in which specific gravity and urine volume were measured over a 6-hour period of water deprivation, no significant differences in specific gravity were observed, but males produced significantly ($p<0.01$) less urine at $\geq$100 mg/ℓ. Females produced

less urine at 200 and 800 mg/ℓ but the difference was significant only at 200 mg/ℓ. In a dilution test, specific gravity and urinary volume measurements over a 2-hour period following a water load of 25 mℓ/kg showed significantly increased specific gravity of urine in males at ≥100 mg/ℓ and in females at ≥200 mg/ℓ, and significantly decreased urinary volume in males at 800 mg/ℓ and females at ≥200 mg/ℓ. Gross and histological examinations of major organs (brain, heart, trachea, liver, spleen, kidneys, stomach, intestine, colon, rectum, pancreas, bladder, uterus, gonads, pituitary, and thyroid) revealed no treatment-related abnormalities. Statistically significant increased relative organ weights were found in brain, liver, spleen, small intestine, cecum, adrenals, gonads, pituitary and thyroid of males at 800 mg/ℓ. The relative weight of the kidneys at ≥200 ppm and the stomach at ≥100 mg/ℓ were also significantly increased for males. Relative kidney weights were significantly increased in females at ≥100 mg/ℓ ($p<0.001$). Females at 800 mg/ℓ had significantly increased relative weights of brain, liver, stomach, small intestine, adrenals and thyroid. No effects were observed at 50 mg/ℓ. These results are similar to those found by Dunlap et al. (1958) but histopathologic changes of the liver were not seen.

In an East German study by Neubauer et al. (1977), available as an English abstract, male rats were treated at oral doses of allyl alcohol of 0.02 or 0.04 mℓ/kg/day for 12-14 weeks. Serum enzyme changes that suggested hepatic injury included increased SGPT and the appearance of mitochondrial GDH. Additional details of the study and further evidence of toxic effects were not available.

In Russian studies (Al'meev and Karmazin, 1969; Karmazin, 1969) available as English abstracts, rats were treated orally at 2.5, 0.05 and 0.005 mg allyl alcohol/kg/day for 6-8 months. No morphological changes were observed in visceral organs of rats exposed at the two lower doses and miscellaneous (unspecified) changes occurred at the higher dose. Additional data regarding treatment-related pathologies were not available. Nervous system toxicity, measured by conditioned reflex activity, was not affected at 0.005 or 0.05 mg/kg for 6 months. Allyl alcohol administered at 2.5 mg/kg for 8 months "weakened the process of stimulation and strengthened the inhibition reaction."

Rabbits were given doses of 2.5, 0.05 and 0.005 mg/kg/day of allyl alcohol in drinking water for 8 months (Al'meev and Karmazin, 1969). No changes in internal organs were seen at the lower two dose levels. Liver hemorrhage and necrosis, dystrophy of the epithelium of the kidney convoluted tubules and splenic diffuse reticular-endothelial hyperplasia were seen at a dose of 2.5 mg/kg/day, suggesting that rabbits are more sensitive than rats to repeated exposure of allyl alcohol.

Dunlap and Hine (1955) and Dunlap et al. (1958) exposed groups of 10 male Long-Evans rats by inhalation to allyl alcohol vapors at levels of 1, 2, 5, 10 and 20 ppm (2.4, 4.8, 11.9, 23.8 and 47.5 mg/m^3)for 7 hours/day, 5 days/week for 60 exposures. Since these exposures produced no gross signs of toxicity, two subsequent experiments using exposures of 40, 60, 100 and 150 ppm (95.0, 143, 238 and 356 mg/m^3) for 7 hours/day, 5 days/week for 90 days were performed. The exposure level of 356 mg/m^3 was lethal with all rats dying within 10 exposures (liver and lung hemorrhage reported). At 238 mg/m^3, 6 of 10 rats died within 46 days with the remainder accidentally killed on the 56th day of exposure. One death occurred after one exposure

at 143 mg/m³ but no deaths occurred among rats exposed at lower levels. Weight gain was significantly ($p<0.05$) retarded in all groups exposed at $\geq$47.5 mg/m³. Eye and nose irritation was evident at exposures of $\geq$95 mg/m³, but at 95 mg/m³, signs of irritation disappeared within a few exposures. Organ-to-body weight ratios showed an increase in lung weight at 95 and 143 mg/m³ and increased kidney weight at 143 mg/m³, but liver-to-body weight ratios were normal. Gross and microscopic changes, including liver and kidney hemorrhage and congestion were reported among rats exposed at 95, 143 and 238 and 356 mg/m³, decreasing in severity with decreasing dose.

Torkelson et al. (1959) exposed groups of male and female rats (n=24 each sex), guinea pigs(n=9 each sex), rabbits (n=3 each sex) and dogs (n=1 each sex) to 2 ppm (4.8 mg/m³) allyl alcohol by inhalation for 7 hours/day, 5 days/week for 180-194 days (6 months). Hematology, growth, mortality, body and organ weights were normal in both sexes of all species when compared with controls. Gross and microscopic examination of tissues (presumed liver and kidney) revealed no treatment-related changes. Exposure to 7 ppm (17 mg/m³) for 5 weeks produced reversible kidney and liver changes in rats, guinea pigs and rabbits. Cloudy swelling, focal necrosis and dilatation of the sinusoids were observed in the liver, and necrosis of the epithelium of the convoluted tubules and interstitial proliferation, which were mild and reversible effects, were found in the kidneys.

5.6. OTHER RELEVANT INFORMATION

The acute toxicity of allyl alcohol has been studied by numerous investigators (Tables 5-2 and 5-3) by various routes of administration. These studies clearly show the propensity of allyl alcohol to produce liver damage, often localized to the periportal regions, after short-term exposure

TABLE 5-2

Effects of Single Dose or Short-Term Exposure to Allyl Alcohol

Route	Species	Dose	Effect	Reference
Oral	rat	4 mg/kg or 9.7 mg/kg for 30 days in diet	Reduced appetite, microscopic liver lesions, death. No effect at 4.0 mg/kg, LD_{50} of 64 mg/kg.	Smyth et al., 1951
Oral	rat	64 mg/kg for 30 days in diet	LD_{50} (a range finding test)	Smyth and Carpenter, 1948
Oral	rat	30 mg/kg for 1, 10 or 28 days	Periportal necrosis associated with decrease of ADH, SDH, benzo[a]pyrene hydroxylose, cytochrome P-450 after a single dose. Further daily administration did not increase effects, prolonged administration showed no effects and regression of original damage, possibly due to modification of hepatic metabolism.	Lake et al., 1978
Oral	rat	25 mg/kg in corn oil for 28 days	No macroscopic liver lesions after 28 days showing development of tolerance, acrolein then infused, (1.7 mg/kg) intraportally producing periportal necrosis.	Butterworth et al., 1978
Oral	rat	14 or 28 mg/kg for 10 days	Engorgement of heart, spleen, liver, kidneys, swelling of convoluted ducts of the kidney, and necrotic changes in heart and liver.	Al'meev and Karmazin, 1969
Oral	rat	50 mg/kg dissolved in sunflower oil animals killed at 12, 24, 48, 72 and 96 hours.	Periportal necrosis by 12-24 hours; pancreatic acidophilia after 12 hours, focal necrosis after 24 hours, vacuolation after 72 hours, decrease in pancreatic ADH.	Nizze et al., 1979
Oral	rat	2% in water, 1/3 of LD_{50} (70 mg/kg) or 25 mg/kg daily for 4 days, sacrificed on 5th day, livers examined	Colorless secretion from eyes, diarrhea, scrawny appearance, death from 4 hours-4 days. Mortality ratio was 0/12 with focal necrotic liver lesions.	Taylor et al., 1964
Oral	rat	0.055 mL/kg twice a week	Liver damage	Vajta et al., 1982
Oral	rat	100 µL/kg bw	Periportal necrosis, reduced prothrombin index after 12 hours, normal after 24 hours; galactose elimination; hepatic glutathione unchanged before 24 hours, then glutathione elevated 2-fold. Reduction of microsomal p-nitro-anisole demethylation.	Poulsen and Korsholm, 1984

TABLE 5-2 (cont.)

Route	Species	Dose	Effect	Reference
Oral	rat mouse rabbit	1% in distilled water rabbit 71; mg/kg LD_{50} mouse; 96 mg/kg LD_{50} rat; 99 mg/kg LD_{50}	Apathy, edema, lacrimation, tremors, convulsions and coma preceding death; lung edema, congestion; discolored necrotic livers, periportal necrosis symptoms not as severe in mice.	Dunlap et al., 1958
Oral	rat	0.4 mL/100 g allyl alcohol as 3.5 vol % solution with 12.8% ETOH, water and pure European and hybrid wines	Percent of necrosis increased when given with wine, values were 27.5% with water, 38.3% with ETOH, 50.9% with pure European and 78.1% with hybrid wines.	Klieve et al., 1960
Oral	rat	0.04 mL/kg	Increase and changes in the fatty acid pattern occurring before morphologic changes in the liver.	Berg et al., 1968
Oral	rat	60 or 120 mg/kg (single dose)	O_2 uptake by liver slices severely inhibited at high dose; O_2 uptake by kidney slices increased at both doses; no effect on O_2 uptake by brain slices.	Kodama and Hine, 1958
Oral	rat	10 mg/100 g, 1% solution	Vacuolization of mitochondrial matrix in hepatocytes after 4 hours; decrease of SDH, glucose-6-phosphatase; increased acid phosphatase, acid DNAase and acid RNAase.	Blugers et al., 1974; Bolotova et al., 1972
Oral	rat	1 mL/100 g, 1% solution	Microsomal cytochrome P-450 increased 33%; increased level of malonic dialdehyde.	Gorshtein et al., 1978
Oral	rat	0.05 mL/kg	Hepatic necrosis after 24 hours, increased levels of transaminases in serum, decrease in hepatic glutathione.	Atzori et al., 1983
Oral	rat	4.0 mL/kg of 0.8% allyl alcohol	Increased levels of SGPT and retention of bromosulfopthalein, periportal necrosis.	Srinivasan et al., 1970
Oral	rat	165 and 310 mg/kg/day for 10 days	Decreased catalase activity, increased number of circulating leucocytes.	Karmazin, 1965
Oral	rabbit	1 mL/kg	Lowered plasma fibrinogen and thromboplastin, increased bilirubin level, increased plasma transaminase and alkaline phosphatase.	Kim, 1970
Oral	rabbit	30 mg	Liver damage but no effect on plasma cholinesterase activity.	Boelke and Poser, 1971
Inhalation	rat	250 ppm	After 4-hour exposure, death in 2/6, 3/6, 4/6 rats	Carpenter et al., 1949

TABLE 5-2 (cont.)

Route	Species	Dose	Effect	Reference
Inhalation	rat rabbit monkey	50, 200, 1000 ppm for 7 hours/day, up to 30 days	Monkey died in 4 hours at 1000 ppm with vomiting, diarrhea, severe pain extensive organ necrosis; rabbits died in 3-4 hours at 1000 ppm with extensive organ necrosis; rats died in 3 hours at 1000 ppm with extensive organ necrosis. At 200 ppm, rats died in 1 or 2 days; rabbits after 1 hour labored breathing, death 3-18 days. At 50 ppm one rabbit died on day 14, the other survived 28 days, both had hemorrhage of GI tract and lungs. Rats died after 30 days. All animals discussed above had liver necrosis.	McCord, 1932
Intraperitoneal	rat	0.05 mL/kg	Changes in liver enzymes (decreased microsomal protein, cytochrome P-450 and oxidase), periportal necrosis with some midzonal involvement.	Gregus et al., 1982
Intraperitoneal	rat induced or noninduced with pentobarbitol	0.05 mL/kg dissolved 1:20 in water	Periportal necrosis, decreased cytochrome P-450.	Gumbrecht and Franklin, 1983
Intraperitoneal	rat	0, 10, 15, 20, 30, 40 mg/kg in 0.5 mL of saline	Increased GPT activity at 20 and 30 mg/kg, no effect with 0-15 mg/kg. All rats died with 40 mg/kg dose. Increase in sorbitol dehydrogenase with 30 mg/kg after 21 hours; fasting protected against hepatotoxic effect.	Hanson and Anders, 1978
Intraperitoneal	rat	0.05 mL/kg	Periportal necrosis after 24 hours.	Reid, 1972
Intraperitoneal	rat	0.036 mL/kg bw (1.8 mL/kg of 2% solution in saline)	Periportal necrosis, changes in hepatic enzymes, serum enzymes liver toxicity, both increased in aged rats.	Rikans, 1984
Intraperitoneal	rat	0.05 mL/kg dissolved in olive oil (10 mL/kg) rats exposed to reduced oxygen for 6 hours	No enhancement of hepatotoxic effect or changes in GOT, GPT, SDH were elevated by allyl alcohol alone.	Strubelt and Breining, 1980
Intraperitoneal	mice	0.1 mL (kg^{-1}) in 1% tylose (10 mL/kg) given to fasted and nonfasted animals	Fasting increased GOT and SDH levels above effects from allyl alcohol.	Strubelt et al., 1981
Intraperitoneal	mice	0.6 mL of 0.3% solution in saline	Periportal necrosis, enhanced antibodies to horse serum, increased susceptibility to anaphylactic shock.	Paronetto and Popper, 1964

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TABLE 5-2 (cont.)

Route	Species	Dose	Effect	Reference
Intraperitoneal	rat	0.05 mL/kg, animals sacrificed at 3, 6, 12 and 24 hours	Periportal necrosis functional derangement of hepatic endoplasmic reticulum after 24 hours, decreased activity of N-demethylation.	Thorgiersson et al., 1976
Intraperitoneal	rat	animals were given microsomal enzyme inducers or inhibitors then allyl alcohol 0.05 mL/kg in corn oil, killed 24 hours later	No significant alteration of liver UDPGA.	Watkins and Klaassen, 1983
Intraperitoneal	rat	0.05 mL/kg	Necrosis but no correlation with negligible increased plasma isocitric dehydrogenase.	Peiter and Klinger, 1973
Intraperitoneal	rat	0.01 and 0.02 mL/kg	Increased SGOT, SGPT; retention of bromosulfophthalein and liver triglycrides.	Strubelt et al., 1970
Intravenous	dog	40 mg/kg (single dose)	Decreased respiratory rate and amplitude; decreased blood pressure, increased hematocrit.	Kodama and Hine, 1958
Intravenous Intraportal Infusion	rat (weanling)	8.5, 17.0 or 22.5 mg/kg	No periportal necrosis with doses of allyl alcohol but doses of 0.425, 0.85 or 1.70 mg/kg of acrolein caused periportal necrosis in 0, 2, 3 rats, respectively; lesions similar to oral administration of allyl alcohol.	Butterworth et al., 1978
Intravenous	rat	1.8 mL/kg of 1:50 solution in saline	Periportal necrosis, changes in liver enzymes (decreased cytochrome P-450, increased glutathione transferase).	James et al., 1981
Subcutaneous	rat	0.5-1.5 mL/kg (single dose)	Changes in liver microsomal, lysosomal and mitochondrial enzymes.	Feuer et al., 1965
NA	rat	NR	Necrotic zones and changes in liver enzymes.	Rusu et al., 1983
Subcutaneous	rat	5 mg of a 2% aqueous solution	Periportal necrosis, no change in pentobarbitol sleeping time.	Balazs and Grice, 1963

NR = Not reported; NA = not available

TABLE 5-3

Results of Single or Short-Term Exposures of Animals to Vapors of Allyl Alcohol*

Concentration (ppm)	Animal	Duration of Exposure (hours)	Outcome	Reference
29,300	rat	0.5	100% lethal	Adams et al., 1940
14,500	rat	1.25	100% lethal	Adams et al., 1940
14,500	rat	0.5	survived	Adams et al., 1940
14,500	guinea pig	0.75	100% lethal	Adams et al., 1940
14,500	guinea pig	0.25	survived	Adams et al., 1940
5,800	rat	2.0	100% lethal	Adams et al., 1940
5,800	rat	0.5	survived	Adams et al., 1940
2,900	rat	3.0	100% lethal	Adams et al., 1940
2,900	rat	1.0	survived	Adams et al., 1940
2,900	guinea pig	2.0	100% lethal	Adams et al., 1940
2,900	guinea pig	1.0	survived	Adams et al., 1940
1,000	monkey	4	death	McCord, 1932
1,000	rabbit	4	100% lethal	McCord, 1932
1,000	rat	4	100% lethal	McCord, 1932
1,060	rat	1	LC_{50}	Dunlap et al.,1958
1,000	rat	1	LC_{67}	Smyth and Carpenter, 1948
500	rat	1	survived	Smyth, 1956
290	rat	8.0	100% lethal	Adams et al., 1940
290	rat	3.0	survived	Adams et al., 1940

TABLE 5-3 (cont.)

Concentration (ppm)	Animal	Duration of Exposure (hours)	Outcome	Reference
290	guinea pig	4.0	100% lethal	Adams et al., 1940
290	guinea pig	1.0	survived	Adams et al., 1940
250	rat	4	some deaths	Carpenter et al., 1949
165	rat	4	LC_{50}	Dunlap et al., 1958
76	rat	8	LC_{50}	Dunlap et al., 1958
200	rat	2x7	100% lethal	McCord, 1932
200	rabbit	18x7	100% lethal	McCord, 1932

*Source: Rowe and McCollister, 1982

by all routes of exposure. Other toxic effects occasionally reported include renal necrosis, pulmonary edema and CNS effects at higher dose levels.

Acute lethality values for allyl alcohol have been reported for various test species exposed by several routes of administration (Table 5-4). Rats, mice and rabbits appear to be equally sensitive to allyl alcohol with most LD_{50} values ~70-90 mg/kg following a single oral dose. Dunlap et al. (1940) reported 1- and 8-hour LC_{50} values at 1060 and 76 ppm, respectively, in rats inhaling allyl alcohol. Dermal LC_{50} values were approximately equal to those reported for oral exposure, suggesting efficient dermal absorption. Likewise, intravenous and intraperitoneal LD_{50} values were within the range of oral LD_{50} values suggesting nearly complete oral absorption.

The effects of allyl alcohol on primary maintenance cultures of adult rabbit hepatocytes were studied by Poole et al. (1982). A dose-response pattern of leakage of GOT and GPT into the medium was observed, indicative of plasma membrane damage.

Cowan et al. (1967) found that allyl alcohol in dosages from 5-25 µl inhibited uptake of iodine-131 by the thyroid of rats and found allyl alcohol to be toxic with 30-350 µl, given by stomach tube. Allyl alcohol had antithyroid activity when uptake of ^{131}Iodine was assessed in rats (Saghir et al., 1967).

Yashuda et al. (1976) found the 50% inhibitory concentration for guinea pig ileum smooth muscle contraction to be 117.8 mM allyl alcohol when induced by 0.4 mM $CaCl_2$. Muir (1983) found the amount of allyl alcohol to block spontaneous contractions of rabbit isolated ileum by 50% (EC50) <u>in vitro</u> to be 0.25.

TABLE 5-4

Acute Lethal Levels for Allyl Alcohol[a]

Route	Species	Dose[b]	Reference
Oral	rat (young male)	105 mg/kg	Dunlap et al., 1958
Oral	rat (adult male)	99 mg/kg	Dunlap et al., 1958
Oral	rat	64 mg/kg	Smyth and Carpenter, 1948
Oral	rat	70 mg/kg	Taylor et al., 1964
Oral	rat	140 mg/kg	Karmazin, 1965
Oral	rat	50 mg/kg	Nizze et al., 1979
Oral	mouse	75.5 mg/kg	Karmazin, 1965
Oral	mouse	96 mg/kg	Dunlap et al., 1958
Oral	rabbit	71 mg/kg	Dunlap et al., 1958
Oral	rabbit	90 mg/kg	Karmazin, 1965
Inhalation	rat	1060 ppm (LC_{50}) (1 hour)	Dunlap et al., 1940
Inhalation	rat	165 ppm (LC_{50}) (4 hours)	Dunlap et al., 1940
Inhalation	rat	76 ppm (LC_{50}) (8 hours)	Dunlap et al., 1940
Inhalation	rat	1000 ppm (1 hour) (4/6 died)	Smyth and Carpenter, 1948
Inhalation	guinea pig	290 ppm (4 hours) (100% lethal)	Adams et al., 1940

TABLE 5-4 (cont.)

Route	Species	Dose[b]	Reference
Inhalation	rabbit	1000 ppm (4 hours) (100% lethal)	Adams et al., 1940
Inhalation	monkey	1000 ppm (4 hours) (100% lethal)	McCord, 1932
Skin	rabbit	53 mg/kg	Smyth and Carpenter, 1948
Skin	rabbit	89 mg/kg	Dunlap et al., 1958
Intraperitoneal	mouse	60 mg/kg	Dunlap et al., 1958
Intravenous	mouse	80 mg/kg	Zagradnik et al., 1962

[a]Source: Rowe and McCollister, 1982; TSCA-ITC, 1984

[b]LD_{50}, unless otherwise specified

Severe irritation to mucous membranes occurs (Browning, 1965). Allyl alcohol at 2 ppm for 1-3 minutes was detected as a definite odor by 5 of 10 human volunteers, but no irritation occurred (Torkelson et al., 1959). All five volunteers reported eye and nose irritaion after exposure to 25 ppm allyl alcohol for up to 5 minutes (Dunlap et al., 1958). Severe irritation and toxic effects have been reported at 25 ppm for the human eye and at 4270 µg for the rabbit eye; application caused transitory corneal opacity in both (Rowe and McCollister, 1982). Rabbit skin irritation occurs with 10 mg/24 hours. Application to uncovered skin causes little local irritation, but absorption is rapid and can occur in toxic and lethal amounts (Rowe and McCollister, 1982). The RD_{50} of allyl alcohol that was due to sensory irritation of the upper respiratory tract was 3.9 ppm (Nielsen et al., 1984). Pitt (1982) reported a vapor hazard index of 11 for allyl alcohol.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The acute lethal concentrations of allyl alcohol have been determined for several species of freshwater fish. The 24-, 48- and 96-hour LC_{50} values for rainbow trout (Salmo gairdneri) were 2.53, 1.45 and 1.28 mg allyl alcohol/ℓ, respectively (Schneider, 1979). The bluegill sunfish (Lepomis macrochirus) appeared almost equally sensitive, having 24- and 48-hour LC_{50} values of 2.65 and 1.50 mg/ℓ, respectively (Schneider, 1979). Bridie et al. (1979b) reported the 24-hour LC_{50} for goldfish (Carassius auratus) as 1.0 mg allyl alcohol/ℓ. In the European rudd (Scardinius erythrophthalmus) the threshold of harmful effects (duration of exposure not specified) was 10 mg/ℓ (Hubault, 1955).

The 48-hour LC_{50} for a marine polychaete, Ophryotrocha diadema, was determined to range between 0.33 and 1.00 mg/ℓ (Parker, 1984).

6.2. CHRONIC EFFECTS

The 14-day LC_{50} for guppies (Poecilio reticulata) was 14 µmol allyl alcohol/ℓ (0.813 mg/ℓ) (Hermens and Leeuwangh, 1982).

Woelke (1961) reported that allyl alcohol at 2.5 mg/ℓ was lethal to bivalve larvae (duration of exposure not specified).

6.3. PLANT EFFECTS

Pertinent data on the toxic effects of allyl alcohol on aquatic plants were not located in the available literature as cited in the Appendix.

6.4. RESIDUE

Pertinent data on the residues of allyl alcohol in the aquatic environment or aquatic organisms were not located in the available literature as cited in the Appendix.

6.5. OTHER RELEVANT INFORMATION

Additional data regarding the toxic effects of allyl alcohol on aquatic organisms were not located in the available literature as cited in the Appendix.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

ACGIH (1983), based on the recommendation of the ACGIH (1980), has adopted a TWA-TLV for allyl alcohol of 2 ppm (5 mg/m³) and STEL of 4 ppm (10 mg/m³) with a "skin" notation. The TLV was based primarily on the effects observed in dogs, rats, guinea pigs and rabbits following inhalation exposure in the study by Torkelson et al. (1959) (see Chapter 5). The TLV and STEL are considered sufficient to provide protection against external and systemic effects (ACGIH, 1980). OSHA has also adopted a TWA-TLV of 2 ppm, but the STEL is 5 ppm (12 mg/m³) (Code of Federal Regulations, 1981).

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of allyl alcohol were not located in the available literature as cited in the Appendix.

8. RISK ASSESSMENT

Data regarding the carcinogenicity of allyl alcohol were not located in the available literature as cited in the Appendix. The results of testing of allyl alcohol for reverse mutations in Salmonella typhimurium are predominately negative. Positive results were obtained without metabolic activation in strain TA100 using a pre-incubation protocol but not in a plate test by Lutz et al., (1982) and marginally positive in a pre-incubation assay using TA1535 strain by Lijinsky and Andrews (1980), while negative results in this strain and other strains were obtained with and without metabolic activation by other investigators (Carere and Morpurgo, 1981; Yamaguchi, 1980). Allyl alcohol was negative for forward mutations in Streptomyces coelicolor and in Aspergillus nidulans (Carere and Morpurgo, 1981; Principe et al., 1981; Bignami et al., 1977).

Hepatic toxicity and a high rate of fetal mortality were observed in the offspring of pregnant mice treated intraperitoneally with an unspecified dose of allyl alcohol on day 18, but not on day 16, of gestation (Roschlaw and Rodenkirchen, 1969). No other pertinent data regarding reproductive effects of allyl alcohol were found in the available literature as cited in the Appendix.

Although no studies of chronic duration were located, an ADI for allyl alcohol can be estimated based on several subchronic studies. As reported in abstracts and reviews of Russian studies (Al'meev and Karmazin, 1969; Karmazin, 1969), rats treated orally at 25 mg/kg/day for 6-8 months had unspecified miscellaneous changes in visceral organs and changes in conditioned reflex activity; rabbits similarly treated had liver hemorrhage and necrosis, dystrophic renal tubules and splenic hyperplasia. In an abstract

of an East German study (Neubauer et al., 1977), doses of 0.02 and 0.04 mℓ/kg/day for 12-14 weeks resulted in increased levels of SGPT and the appearance of mitochondrial GDH in the serum. Assuming that the specific gravity of allyl alcohol (see Section 1.2.) approximates the density, 0.02 and 0.04 mℓ/kg/day are equivalent to ~17 and 34 mg/kg/day. The lack of adequate reporting of experimental protocol and description of effects precludes use of these studies for risk assessment.

Rats treated with allyl alcohol in the drinking water for 90 days had decreased body weights, possibly associated with reduced water intake, and decreased amounts of peritoneal fat at 500 and 1000 mg/ℓ (Dunlap et al., 1958). Females at 1000 mg/ℓ had gross and histologic evidence of liver damage, such as yellow discoloration and necrosis with evidence of regeneration. At $\geq$250 mg/ℓ, rats had significantly ($p<0.05$) increased relative liver or kidney weights or both. No effects were observed at $\leq$100 mg/ℓ. Based on water consumption data, 100 mg/ℓ was equivalent to 11.6 and 13.2 mg/kg/day for males and females, respectively.

In another study (Carpanini et al., 1978), rats treated at drinking water concentrations $\geq$200 mg/ℓ for 15 weeks had depressed growth and reduced food consumption. Renal function was impaired, as evidenced by significantly increased specific gravity of urine in a urine dilution test at $\geq$100 mg/ℓ and significantly decreased urinary output at $\geq$100 mg/ℓ in a concentration test and at $\geq$200 mg/ℓ in the dilution test. Relative weights of many organs were significantly increased at 800 ppm and the relative weight of the kidneys was significantly increased in males at $\geq$200 mg/ℓ and females at $\geq$100 mg/ℓ. No effects were observed at 50 mg/ℓ.

Two subchronic inhalation studies were also available. Torkelson et al. (1959) found no effects in rats, guinea pigs, rabbits or dogs exposed to

allyl alcohol vapor at 2 ppm (4.8 mg/m³), 7 hours/day, 5 days/week for 6 months; but rats, rabbits and guinea pigs exposed at 7 ppm (17 mg/m³), 7 hours/day, 5 days/week for 5 weeks had microscopic evidence of liver necrosis and glomerulonephritis.

Dunlap et al. (1958) found no effects in rats exposed at ≤10 ppm (≤23.8 mg/m³), 7 hours/day, 5 days/week for 90 days. At ≥20 ppm (47.5 mg/m³), weight gain was depressed. At ≥40 ppm (95 mg/m³), eye and nose irritation occurred, relative lung weight was increased and there was a dose-related increased severity of liver and kidney lesions (hemorrhage and congestion). Exposures ≥60 mg/m³ resulted in death.

Although it is possible to estimate an ADI from inhalation data, for the purposes of this profile, it is more appropriate to derive the ADI from the subchronic drinking water studies.

The study of Carpanini et al. (1978) provides both the NOEL and the LOAEL for oral exposure to allyl alcohol. Based on actual drinking water consumption data, the investigators calculated that the LOAEL of 100 mg/ℓ, at which relative kidney weight was increased in female rats and renal function was impaired in male rats, was equivalent to dosages of 8.3 and 6.9 mg/kg/day, respectively. The NOEL of 50 mg/ℓ was equal to 4.8 and 6.2 mg/kg/day for males and females, respectively. Although the dosage in female rats is the higher NOEL, 6.2 mg/kg/day is too close to the LOAEL of 6.9 mg/kg/day for use as the basis of the ADI. Using the NOEL of 4.8 mg/kg/day in males and an uncertainty factor of 1000 (10 for interspecies extrapolation, 10 to approximate chronic exposure and 10 to protect the most sensitive individuals of the human population), an ADI of 0.0048 mg/kg/day, or 0.34 mg/day for a 70 kg man, is derived.

9. REPORTABLE QUANTITIES

9.1. REPORTABLE QUANTITY (RQ) RANKING BASED ON CHRONIC TOXICITY

Chronic toxicity data regarding allyl alcohol were not available; therefore, the CS and RQ values have been determined using subchronic toxicity data corrected for long-term exposure. An RQ value of 100 with a CS and human MED of 28 and 3.54 mg/day, respectively, has previously been determined (U.S. EPA, 1983). A summary of the CS and RQ values based on available subchronic toxicity data is listed in Table 9-1.

The human MEDs from oral doses were calculated by multiplying the rat dose in units of mg/kg/day by the cube root of ratio of the body weight of a rat (assumed to be 0.35 kg) to the body weight of a man (assumed to be 70 kg) and by the human body weight. For the inhalation studies, all exposures were for 7 hours/day and 5 days/week. The human MEDs for inhalation exposure were calculated from the expression: MED = mg/m^3 x 7 hours/24 hours x 5 days/7 days x animal ventilatory volume ÷ animal body weight x $\sqrt[3]{\text{animal body weight} \div \text{human body weight}}$. Since all the oral and the inhalation studies were subchronic, an uncertainty factor of 10 was applied to approximate the chronic MED.

The effects of subchronic oral and inhalation exposure of animals to allyl alcohol were discussed in Section 5.5. Abstracts and reviews of studies from the Russian and East German literature (Al'meev and Karmazin, 1969; Karmazin, 1969; Neubauer et al., 1977) reported effects in rats and rabbits at oral doses $\geq$2.5 mg/kg/day, but these studies are not appropriate for use in the RQ derivation because of inadequately described experimental design and inadequate detail in descriptions of reported effects.

TABLE 9-1

Composite Scores for Toxicity of Allyl Alcohol

Route	Species	Dose/Exposure	Chronic Human MED* (mg/day)	RV_d	Effects	RV_e	CS	RQ	Reference
Oral	rat	100 mg/ℓ for 105 days (6.9 mg/kg/day)	8.3	4.1	Increased kidney weight	4	16.4	1000	Carpanini et al., 1978
Oral	rat	100 mg/ℓ for 105 days (8.3 mg/kg/day)	9.9	4.0	Impaired renal function	7	28	100	Carpanini et al., 1978
Oral	rat	1000 mg/ℓ for 90 days (67.4 mg/kg/day)	80.7	2.6	Liver necrosis	6	15.6	1000	Dunlap et al., 1958
Inhalation	rat	95 mg/m³, 7 hours/day, 5 days/week for 90 days	15.1	3.7	Macroscopic evidence of lung hemorrhage, microscopic congestion of lungs and livers	5	18.5	1000	Dunlap et al., 1958
Inhalation	rat	47.5 mg/m³, 7 hours/day, 5 days/week for 90 days	7.6	4.2	Decreased body weight gain	4	16.7	1000	Dunlap et al., 1958
Inhalation	rat	17 mg/m³ 7 hours/day, 5 days/week for 35 days	2.7	4.9	Cloudy swelling, focal necrosis and dilatation of sinusoid of liver; necrosis of renal tubule epithelium	6	29.1	100	Torkelson et al., 1959
	guinea pig	same as above	0.9	5.6	Same as above	6	33.4	100	Torkelson et al., 1959
	rabbit	same as above	4.1	4.6	Same as above	6	27.5	100	Torkelson et al., 1959

*The subchronic doses and exposures were divided by an uncertainty factor of 10 to approximate a chronic MED.

Carpanini et al. (1978) reported increased kidney weight in female rats and impaired renal function (significantly increased specific gravity and decreased urinary output in water loading and water deprivation experiments) in male rats exposed to allyl alcohol in the drinking water at 100 mg/ℓ. Based on water consumption data, the investigators calculated that 100 mg/ℓ was equivalent to 6.9 mg/kg/day for females and 8.3 mg/kg/day for males. The MED corresponding to 6.9 mg/kg/day is 8.3 mg/day, and the corresponding RV_d is 4.1. Increased kidney weight warrants an RV_e of 4. The product of the RV_d and the RV_e is a CS of 16.4, with a correspond , RQ of 1000. The MED calculated from the animal dose of 8.3 mg/kg/day is 9.9 mg/day, corresponding to an RV_d of 4.0. Impaired renal function warrants an RV_e of 7, the CS is 28 and the RQ is 100.

The drinking water study conducted by Dunlap et al. (1958) reported increased liver and kidney weights in rats exposed at $\geq$250 mg/ℓ for 90 days. Since increased organ weights occurred at a lower exposure level in the Carpanini et al. (1978) study, no CS is determined for increased organ weights at 250 mg/ℓ. At 1000 mg/ℓ (67.4 mg/kg/day, calculated by the investigators from drinking water consumption data), female rats had liver necrosis (Dunlap et al., 1958). The MED calculated from 67.4 mg/kg/day is 80.7 mg/day, corresponding to an RV_d of 2.6. The RV_e for liver necrosis is 6, the CS is 15.6 and the RQ is 100. This study was not considered in the previous derivation of the RQ (U.S. EPA, 1983) because only a brief review (Browning, 1965) of the Dunlap et al. (1958) drinking water study was available at that time.

In the 90-day inhalation study of Torkelson et al. (1959), no effects in rats, rabbits, guinea pigs and dogs were observed at the only concentration (2 ppm or 4.7 mg/m^3) tested. In the shorter inhalation study by Torkelson

et al. (1959), a concentration of allyl alcohol of 7 ppm (17 mg/m³), 7 hours/day, 5 days/week for 35 days produced focal necrosis in livers and kidneys of rats, rabbits and guinea pigs. The human MEDs of 2.7, 0.9 and 4.1 were calculated for rats, guinea pigs and rabbits, respectively, corresponding to RV_ds of 4.9, 5.6 and 4.6. An appropriate RV_e, reflecting focal necrosis, is 6. The CSs are 29, 33 and 28, respectively, and correspond to RQs of 100.

In the inhalation study of Dunlap et al. (1958), concentrations $\geq$142.5 mg/m³ for 7 hours/day, 5 days/week for 90 days resulted in the death of rats, as well as eye discharge, respiratory irritation, decreased weight gain and increased relative liver and kidney weights. The deaths occurred after only a few exposures and, therefore, represent acute effects of high exposure. No deaths occurred at $\leq$95 mg/m³. At $\geq$95 mg/m³, 7 hours/day, 5 days/week, rats had hemorrhagic and congested lungs and livers. The MED is 15.1 mg/day and corresponds to an RV_d of 3.7. The effects warrant an RV_e of 5, the CS is 19 and the RQ is 1000. At $\geq$47.5 mg/m³, rats had decreased body weight gain. The MED is 7.6 mg/m³, the RV_d is 4.2, the RV_e is 4 and the CS is 16.7. The corresponding RQ is 1000. The U.S. EPA (1983) did not rank the effects in the inhalation study of Dunlap et al. (1958) because only brief reviews by Torkelson et al. (1959) and Browning (1965) were available at that time.

Reviewing the available CS and RQ values for allyl alcohol (see Table 9-1), it is evident that both the oral study by Carpanini et al. (1978) and the inhalation study by Torkelson et al. (1959) result in CS values of 28 and RQ values of 100. The U.S. EPA (1983) previously dismissed the renal toxicity data reported by Carpanini et al. (1978) since the affected rats also had decreased water consumption that may have caused the renal effects.

The development of renal toxic effects in animals exposed to allyl alcohol, however, is supported by inhalation studies and acute toxicity studies (see Section 5.6.). In addition, the drinking water study by Carpanini et al. (1978) was conducted for 15 weeks while the inhalation study was conducted for only 5 weeks. Toxic effects occurring after 15 weeks of exposure should more closely approximate the chronic toxicity of allyl alcohol. Therefore, an RQ of 100 pounds based on the study of Carpanini et al. (1978) is now recommended (Table 9-2).

9.2. WEIGHT OF EVIDENCE AND POTENCY FACTOR ($F=1/ED_{10}$) FOR CARCINOGENICITY

Pertinent data regarding the carcinogenicity of allyl alcohol were not located in the available literature as cited in the Appendix. The results of the testing of allyl alcohol for reverse mutations in Salmonella typhimurium are equivocal. Lutz et al. (1982) found allyl alcohol to be positive in strain TA100 and Lijinsky and Andrews (1980) obtained positive results in at TA1535. Other studies (Carere and Morpurgo, 1981; Principe et al., 1981; Yamaguchi, 1980; Bignami et al., 1977), however, found negative results in TA100 and other strains of S. typhimurium and negative results for forward mutation in Streptomyces coelicolor and Aspergillus nidulans (see Section 5.2.).

Until additional evidence regarding the carcinogenicity of allyl alcohol becomes available, it is not possible to determine a potency factor (F-factor) for the compound. According to the IARC (1982) classification of chemicals for carcinogenic potency, allyl alcohol is a Group 3 compound.

TABLE 9-2

Allyl Alcohol

Minimum Effective Dose (MED) and Reportable Quantity (RQ)

Route:	oral
Dose*:	9.9 mg/day
Effect:	impaired renal function
Reference:	Carpanini et al., 1978
RV_d:	4.0
RV_e:	7
Composite Score:	28
RQ:	100

*Equivalent human dose

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320
TOXLINE
RTECS
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE
TSCAPP

These searches were conducted in November, 1984 with the exception of the TOXLINE, which was searched in August, 1984 and was kindly supplied by Dynamac Corp. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981, 1982, 1983). Cincinnati, OH. 486 p.

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USITC (U.S. International Trade Commission). 1983. Synthetic Organic Chemicals. U.S. Production and Sales, 1982, USITC Publ. 1422. Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.

Worthing, C.R. and S.B. Walker, Ed. 1983. The Pesticide Manual. British Crop Protection Council. 695 p.

In addition, TSCA 8e submission 8EHQ-0181-0381 86-8000168 was reviewed.

In addition, approximately 30 compendia of aquatic toxicity data were reviewed, including the following:

Battelle's Columbus Laboratories. 1971. Water Quality Criteria Data Book. Volume 3. Effects of Chemicals on Aquatic Life. Selected Data from the Literature through 1968. Prepared for the U.S. EPA under contract No. 68-01-0007. Washington, DC.

Johnson, W.W. and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Summaries of Toxicity Tests Conducted at Columbia National Fisheries Research Laboratory. 1965-1978. USDI, Fish and Wildlife Service Resource Publ. 137, Washington, DC.

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